REMARKS

A new inventor declaration was submitted with the last response.

The rejection of claims 1-30 under 35 U.S.C. § 112, second paragraph, is moot in light of the foregoing amendment.

The rejection of claims 11-30 under 35 U.S.C. § 103 over Nagabhushan in view Kruse is respectfully traversed.

The present invention relates to a pharmaceutical composition which is an aqueous injectable suspension containing micronized florfenicol at a concentration of up to 500 mg/ml in which the composition does not contain organic solvent. As pointed out in the opening paragraphs of this application, injectable formulations of this drug were known in the art but they contained organic solvents or mixtures of water and organic solvent. The reason organic solvents were used was that florfenicol has a low solubility in water which is enhanced by the presence of the organic solvents. The claimed invention is based, *inter alia*, on the finding that the organic solvent makes the florfenicol susceptible to hydrolyzation because of the increased dissolution but aqueous solutions free of organic solvents do not hydrolyze micronized florfenicol.

The Nagabhushan reference is at best confirmatory of the prior art described in the application. It describes various florfenicol formulations including aqueous formulations as pointed out in a prior Office Action, but all such aqueous composition also contain organic solvents. For example, formulation 1 noted by the Examiner is an oral suspension which contains 5% by weight of propylene glycol and is not intended for use as an injectable. Formulation 5, also noted by the Examiner, is not a suspension

as here claimed, but is a solution in which the drug is dissolved in 500 mg/ml of N,N-dimethylacetamide. There is nothing in this reference which teaches or suggests the presence of micronised florfenicol or a substantially water-insoluble complex, or salt thereof (in any concentration) in an aqueous injectable suspension which is free of organic solvents. All aqueous florfenicol formulations in this reference contain an organic solvent.

The Advisory Action asserts that the Nagabhushan teaches at column 7, line 27 to column 8, line 5 that florfenicol can be reacted with dialkylamine sulfur trifluoride in an inert organic solvent and defines such "organic" solvents as including "inorganic" solvents. It is respectfully pointed out that this characterization is not correct in several respects.

First, what is being reacted with the dialkylamine sulfur trifluoride fluorinating agent is not florfenicol but instead is a protected starting compound in which the primary 3-OH function is protected (col. 7, lines 55-59). An "inert organic" solvent (preferably in tetrahydrofuran, dioxane or tetrahydropyran) is used during the fluorination of this precursor compound, which after deprotection of one group, is further reacted with another material in the presence of, for instance, a lower alkanol. The end product is then isolated and purified by removing the solvents and treating the residue (col. 8, lines 58-63). Thereafter the product is formulated for various modes of administration but none of the formulations disclosed are both aqueous and lack the presence of an organic solvent.

Second, the skilled person reading the description would consider the reference to "inorganic" solvents to be a printing error. To characterize an "organic"

material as including "inorganic" materials makes no sense whatsoever. The skilled person knows that inorganic materials are not organic. All of the solvents actually disclosed are organic, and the skilled person would read the disclosure as being limited to solvents which are organic and ignore the obvious error.

Third, even if the term "inert organic" solvent was considered to include "inorganic" solvents, the actual definition of this solvent in the reference does not include water. That definition requires the entity being used as a solvent to be inert and also to dissolve not only the starting compound but the reagents (including the fluorinating agent). See column 8, lines 1-4. The fluorinating agents in this reference function to replace a hydroxyl group with fluorine; since water contains a hydroxyl moiety, that would likewise be replaced by fluorine (resulting in producing HF). This is well known in the art, as well as being self-evident. Since water is not inert here as it reacts with the fluorinating agent, it is not included within the class of solvents that Nagabhushan teaches can be used.

It is respectfully submitted that it is clear from the foregoing that Nagabhushan does not teach or suggest an aqueous suspension of flurfenicol which does not also include an organic solvent. The instant claims require a composition free of organic solvent.

The Kruse reference has been cited to teach various aspects of the claims but not to teach or suggest an injectable suspension flurfenicol which lacks organic solvent. Accordingly, the basic deficiency in Nagabhushan is not eliminated by modifying that reference by Kruse.

Because of the basic deficiencies in the combination of references discussed above, it is not necessary to address any of the other contentions made in the rejection. Nevertheless, the lack of response should not be taken as acquiescence but is merely an indication that the assertions made are moot.

In light of the foregoing considerations, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited.

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